

☼ Mycobacterial ☼

TB

- D.F
- pathogenesis
- Histopathology
- classification
- stages of granuloma formation
- Tuberculin Test
- BCG vaccine
- Types & Chancre
 - 2. warty "verruosa"
 - 3. Scrofuloderma
 - 4. Cutis orificialis
 - 5. Lupus vulgaris
 - 6. Tuberculous Gumma
 - 7. Acute miliary T.B
- Immunopathology
- spectrum

- Diagnosis
- treatment
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 - papulonecrotic Tuberculoid
 - lichen scrofulosum
 - Erythema induratum
- Atypical mycobacteria
- Swimming pool Granuloma
- M. Ulcerans (Buruli ulcer)

Leprosy

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- mode of infection
- Genetic predisposit
- pathogenesis
- Skin Diseases Based on TH1, TH2
- spectrum
- Classification
- Leprosy in children
- Types: Jere,
 - Indeterminate
 - Tuberculoid
 - Lepromatous
 - Borderline
- Histoid leprosy
- Histogenesis
- HIV + leprosy
- Nature of immune Deficiency in LL
- Reaction leprosy
- Diagnosis
- Ht of leprosy
- Erythema nodosum
- Erythema induratum of Bazin
- Scrofuloderma — lichen scrofulosum
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• Cutaneous Tuberculosis •

- Caused By: M. Tuberculosis
- acid - alcohol fast Bacillus

- Exogenous exposure:

Produce → T.B chancre
→ T.B verrucosa Cutis

- Endogenous infection:

lead to → Scrofuloderma
→ miliary T.B
→ LV

- L.V (Lupus vulgaris):

• Site :- Face - Neck
• lesion "plaque" Apple Jelly"
nodules → Scar still
contain active lesions
"Unhealthy scar"

• Diascopy Test :-
pressing LV lesion on glass
slide → yellowish brown
spots "Apple Jelly"

- Tuberculids:

papulo - Necrotic - lichen
Scrofulosurm - Erythema
induratum

* D.F • Rare Disease 1% of extra pulmonary T.B, 4% of All T.B
• Risk of infection ↑↑ By ↓↓ CMI e.g → long term Ht & cytotoxics
OR Steroids
→ lymphomas, Malnutrition

* pathogenesis:

• Transmitted By → Inhalation of infected Droplets nuclei From
Ptn & Active pulmonary T.B

• Cutaneous T.B → By Direct inoculation of organisms into skin
By → Hematogenous Spread from an internal site of infection
(lung)

• Tuberculous Tissue Reaction triggered when T. lymphocytes previously
sensitized By M. Tuberculosis → Come in contact with specific
Tuberculous antigen

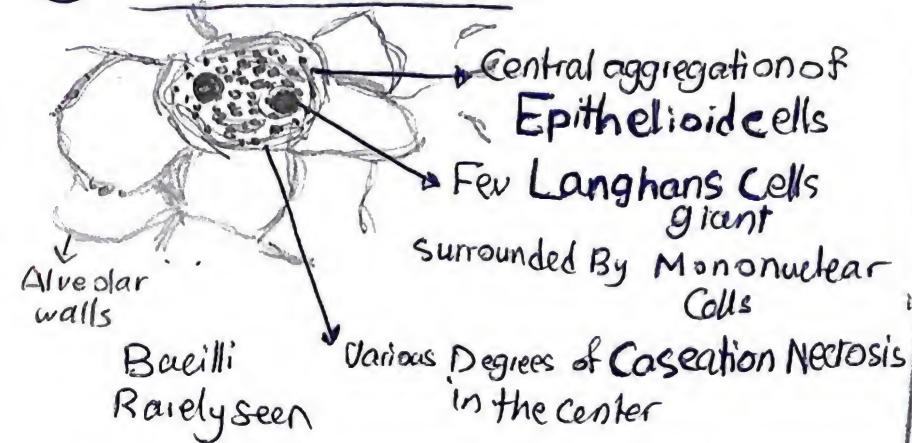
• This leads to → Activation of T. cells + Secretion of Cytokines
which attract Macrophages from circulation → enable them to Kill ingested
Mycobacteria → Granuloma formation → enable them to Kill ingested
Mycobacteria → tense Caseous Tissue necrosis (T.B.)

The outcome of infection depend on:

1. number + virulence of Bacilli
2. Route of infection
3. Natural Resistance
4. Immunological Response of Host

* Histopathology:

① Tuberculous infiltrate



* mononuclear cells → Blood Derived Monocytes
 Develop into Macrophages → give Rise to
Epithelioid cells → some fusing →
 Multinucleated giant cells

② Atypical Tubercles:

- Absence of Necrosis
- Called "Tuberculoid infiltrate"
- present in
 - Syphilis
 - Tuberculoid leprosy
 - Atypical Mycobacteria
 - Rosacea
 - lupus miliaris Disseminatus faciei
 - F.B granuloma

* Classification of Cut. T.B:

① inoculation T.B From Exogenous Source:

- chancre
- verrucosa Cutis
- lupus vulgaris

② 2ry T.B From Endogenous Source

- contagious spread: Scrofulodema
- Autoinoculation orificial T.B

③ Hematogenous

- lupus vulgaris
- Acute Miliary T.B
- T.B gumma

④ Eruptive T.B (Tuberculoid)

- papulo-necrotic
- lichen Scrofulosorum
- Erythema induratum

* Stages of granuloma Formation in T.B:

① initial stage → Expansion of Mycobacterial population in absence of adaptive immunity

→ Mycobacterial multiplication + spread facilitated
By: • Formation of nascent granuloma

→ infected Macrophages → undergo apoptosis → Recruit additional Macrophages → phagocytose Remnants of infected cells and their contents

→ Some of These Newly infected Macrophages → seed dry Granuloma formation

→ adaptive immunity occur → CD4 - CD8 effector T. cells Curtail → Mycobacterial growth

* Tuberculin Test:

- Depend on: Delayed Type Hypersensitivity to Tubercle Bacilli or their products
- Caused By: Infiltration of skin By Sensitized lymphocytes
- The Test: applied By Intracutaneous injection of **5 PPD** (5 units of purified protein Derivative) of Tuberculin Containing Tuberculo proteins (Mantoux Test)
 - the test is read at 48-72 hrs
 - Induration ≥ 10 mm → strongly suggest: past or present Tuberculous Infection
- Tuberculin Sensitivity → appear after 3-6 weeks of onset of M. Tuberculosis Infection (Life long)
- Cross Reaction may occur

* BCG Vaccine:

Bacillus **C**almette **G**uerin → living attenuated Bovine Tubercle Bacillus used to enhance Immunity in T.B -ve

• Cut. Complications of BCG vaccine:-

- 1- Specific:
 - excessive ulceration or lymphadenopathy
 - LV at site of vaccination
 - lichen scrofulosorum
 - papular Tuberculids - lichen nitidus
- 2- Non Specific:
 - Eczema - Keloids - Urticaria - Erythema. Multi
 - Erythema nodosum
 - in **AIDS** pts → BCG Can Cause progressive mycobacteriosis
 - in **ARC** Pts → BCG might Drive them into Terminal

* Types:

- 1- Iry Inoculation Chancre
- 2- Verrucosa Cutis warty
- 3- Scrofuloderma
- 4- Cutis Orificialis
- 5- lupus Vulgaris
- 6- Tuberculous gumma
- 7- Actemiliary T.B

[3]

1 Iry Inoculation Chancere	2 Verrucosa Cutis "warty"	3 Schrofuloderma	4 Cutis orificialis
<p>D.P: Rare - Result from Exogenous Direct inoculation into skin of individual Not previously infected - mainly children "Ghon's Focus"</p>	<p>Result from: Exogenous Direct inoculation into skin of individual with High Degree Immunity e.g: accidental in physicians Verruca necrogenica</p>	<p>Result from: Direct Extension to Skin from underlying Focus • lymph Node - cervical • Bone axillary • Joints</p>	<p>- Occur in: Mucosa or skin adjoining Orifices in ptn & advanced internal T.B • pulmonary • intestinal • Autoinoculation • adult male & Bad general condition</p>
<p>Clinically: Site: Face or extremities Lesion: Asymptomatic - Brownish Red <u>papule</u> or <u>nodule</u> that erode → Indurated non tender <u>ulcer</u> & Sharp Demarcated "undermined edges" - Prominent Regional L.N Healing: several weeks & Scar enlarged glands persist Tuberculin test - Ve early + Ve after 6 weeks</p>	<p>Site: Hands - knees - ankles Lesion: Asymptomatic papule slowly evolves into Warty Hyperkeratotic irregular Papule → Enlarge. By peripheral extension. - Verrucous surface → fissure from which pus expressed - No Regional lymphadenopathy</p>	<p>- Lesion: Bluish-Red nodule → Breaks Down to Form Ulcer & Bluish undermined edges - Floor → covered & Soft granulation Tissue - Numerous Sinuses and Fistula present - Scarring → irregular adherent masses - Healing: puckered scar</p>	<p>painful shallow Ulcer & Bluish undermined edges - rarely exceed 2cm - Healing: No tendency to heal spontaneously - Site: around mouth anus, genitalia</p>
<p>Histopathology: - Early: Acute non specific Neutrophilic Reaction & area of Necrosis ↑ tubercle Bacilli - 3-6 wks later: infiltrate become Granulomatous & epithelioid cells & giant cells lymphocytes Necrosis & sparse Bacilli</p>	<p>Marked: Hyperkeratosis Acanthosis - papillomatosis - Pseudoepitheliomatous Hyperplasia - Superficial dermal Abscess - Intense mixed infiltrate & some giant cells - Only sparse Foci - Bacilli → Rarely seen</p>	<p>- Tuberculous granulation Tissue - Caseation necrosis in Deeper tissue - Bacilli found occasionally</p>	<p>- Non specific inflammatory Reaction - Many Tubercle Bacilli - Prominent Caseation necrosis</p>

5 Lupus Vulgaris : LV

1-D.F: most common Type.

- Start: in Childhood
- Progresses → v. Slowly
- Cocurin: persons e moderate or ~~low~~ High Degree Immunity
- Tuberculin test → +++
- Site: arise at site of primary inoculation By: Direct extension from underlying infected glands OR By: Hematogenous Spread from obscure origin

2 - Clinically :

- Site: Face, neck (90%) - Buttocks, limbs
- lesion: Sharply Demarcated Serpiginous Reddish-Brown Soft plaque
- Composed of Deep seated nodules

- Slow peripheral extension → leading to thin, contractile unhealthy scar
- Scarring, Destruction of underlying structures → Nose
→ Ear Cartilage
(new lesions at area of Atrophy)

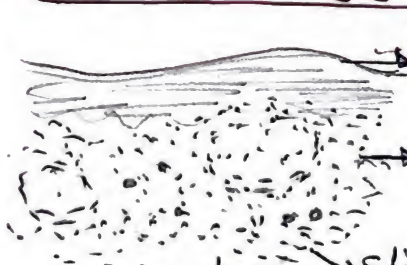
→ SCC, BCC (Less common) → Develop at the Margin

→ Mucosal involve → nasal, Buccal, conjunctiva → may occur

3- Diascopy Test:

- pressing of L.V lesion e glass slide to ↓↓ Vascularity
- yellowish-Brown Spots "apple jelly" nodules

4- Histopathology:

- 
- Epidermal changes: Atrophy - ulceration - Hypertrophy
 - pseudoeplitheliomatous Hypertrophy
 - Epithelioid cells + Langhans giant cells embedded in Dense mononuclear cells ← lymphocytes monocytes
 - Slight or Absent of Caseation Necrosis
 - T.B Bacilli → Difficult to Demonstrate

6 Tuberculous gumma

- Result from: Hematogenous Dissemination From 1ry Focus During Periods of Lower Resistance
- lesion: single or multiple S.C Nodules → Break Down → Form undermined Ulcer or Sinuses

7 Acute military T.B

- D.F: Fatal Disease affect Childs and inFants or immuno-suppressed Adults
- lesion: generalized Erythematous papules, pustules x Ulcers
- internal T.B → Tuberculin - ve

* Immunopathology:

- 2ry Cut T.B Forms a Continuous immuno pathologic Spectrum → Extending from LV through TVC and SF to TCO

- LV → Represent the "High immune" pole with Active CMI and Normal humoral immunity
- SF + TCO → Represent "Impaired CMI" pole e' predominantly humoral immune Response
- LV granuloma → lymphocytic preponderance (active CMI)
 - absent or scanty T.B Bacilli
 - absent / slight Caseation Necrosis
- SF + TCO → relative depletion of lymphocytes (Impaired local immunity)
 - frequent giant cells e' many Bacilli
 - Regular presence of Caseation necrosis

* Spectrum of Cut. T.B :-

The spectrum of cutaneous TB ²

	LV	TVC	SF	TCO	Miliary TB	TB chancre	Tuberculids
Mode of infection	Inoc./Hemat.	Inoc.	Config. spread	Autoinoc.	Hemat.	Inoc.	Hemat.
Tuberculin	+++		++	±	-	- → +	++
AF bacilli	±		++	+++	+++	+++ → ++	-
Caseation necrosis	±		++	+++	+++	+++ → ++	++

* Diagnosis:

1- Tuberculin skin test

2- IFN- γ Release assays: (QuantiFERON T.B. Gold), TSPOT)

These assay \rightarrow Determine if exposure to Recombinant peptides from M. Tuberculosis

Stimulate IFN- γ production
By T-Cells within pt's Blood Sample

ESAT-6
TB7.7
CFP-10

- this assay has great specificity and similar sensitivity compared to Tuberculin skin tests.

- may be used in place of Tuberculin skin test in all situations

- Tuberculin skin Test \rightarrow preferred in Children < 5 yrs

- IFN γ release assay \rightarrow preferred in pt's

* groups that historically have Low Rates of Returning for 2nd visits

(e.g.) \rightarrow homeless
 \rightarrow Drug users

* individuals who have Received BCG

* A Diagnosis of TB Cutis:

Absolute Criteria

1- +ve Culture on Lowenstein Jensen's media from lesion

2- Guinea pig inoculation

Relative "unreliable" Criteria:

1- clinical history, signs

2- presence of Active proven TB focus elsewhere in Body

3- presence of acid-fast Bact. in lesion itself

4- Histopathology

5- +ve reaction to tuberculin

6- Effect of specific therapy

\rightarrow Multi bacillary : \rightarrow pauci bacillary

1- Tubercles chancre

2- Scrofuloderma

3- Tuberculosis orificialis

4- Acute milium T.B

5- Gumma T.B

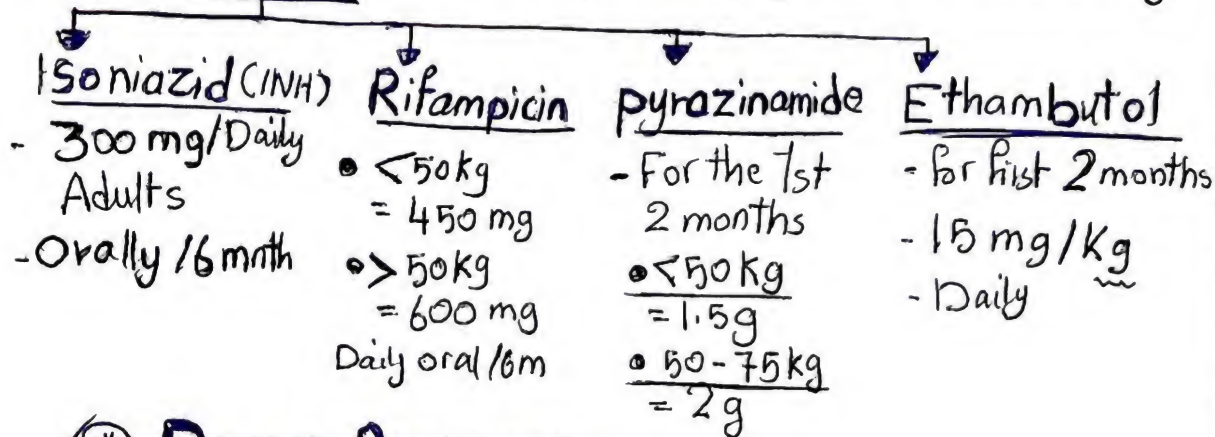
1- Tuberculosis Verrucosa Cutis

2- Lupus vulgaris

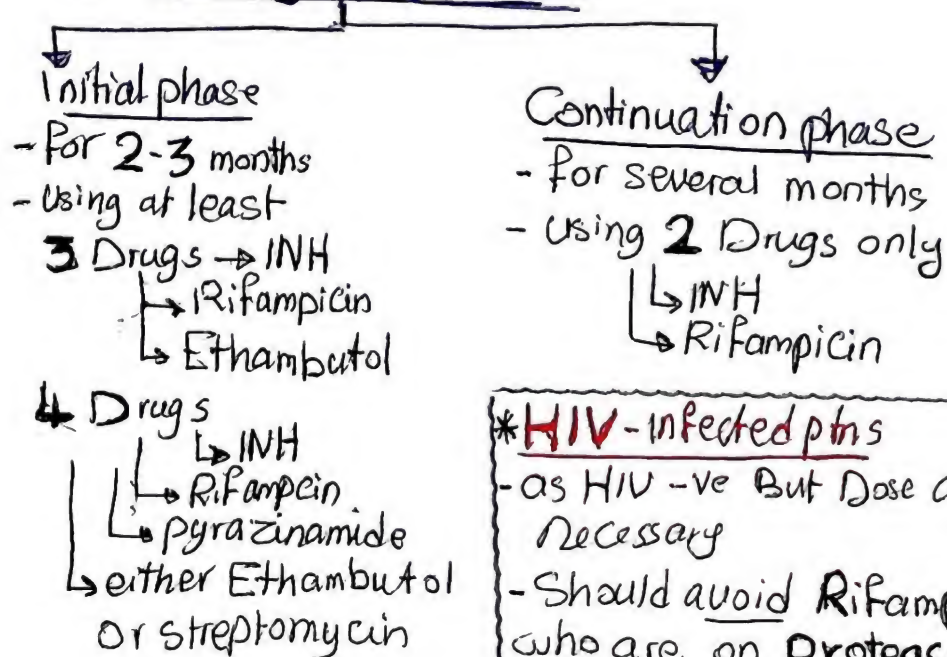
3- Tuberculoids

* Treatment:

(*) Drugs :- All Drugs on empty stomach once daily



(*) Drug Regimens :-



* HIV-infected ptns

- as HIV -ve But Dose adjustments Necessary
- Should avoid Rifampin in ptns who are on protease inhibitors

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* Ptns Receive Pyrazinamide Should undergo Baseline and periodic Serum Uric Acid assessments

* Ptn Receiving Long term Ethambutol Should undergo Baseline and periodic Visual Acuity and Red-green color Precipitation Test

* Calciferol vit D2 150000 U
Toxic Dose For LV ← For 5 Days a week

- acting on the tissue Not the Bacilli
- promoting fibroblasting proliferation and strangling the tubercles

* Surgical treatment:

- excision of small lesions of LV or Warty T.B
- plastic surgery for mutilation and Deformity

* Pregnant women's Active T.B

- Should Be treated even in first stage of pregnancy
- INH - Rifampicin - Ethambutol - pyrazinamide
- Streptomycin Should Not used

*Multi Drug-Resistant TB MDR-TB

- 1- Resistant to INH and Rifampicin [the most two effective]
- 2 - 4% of all new T.B Cases
- 3 - when MDR-TB → start ~~the~~ empirically Before Culture Results Become available Then modify the Regimen as necessary
- 4 - Never add a single new Drug to failing Regimen

- Administer at least 3 (prefer 4-5) of following medications:

- 1 - Aminoglycoside: Streptomycin
Amikacin
kanamycin
2. Fluoroquinolone: Levofloxacin
Ciprofloxacin
Ofloxacin
- 3 - thioamide: Ethionamide
Prothionamide
- 4 - pyrazinamide
- 5 - Ethambutol
- 6 - para-aminosalicylic acid
- 7 - Rifabutin

*Extensively Drug-Resistant tuberculosis:

1. Resistant to INH and Rifampin
2. Resistant to quinolones → the most effective 2nd line Drugs
- 3 - Resistant to at least one of three injectable 2nd-line Drugs: - Amikacin
- Kanamycin - Capreomycin

*Tuberculids *

- Result from: Hematogenous Dissemination of tubercle Bacilli → from Distant source
 - leading to: Delayed type hypersensitivity Response in persons with High Degree of CMI
 - The original TB Focus: Not active at time of Eruption
 - The Bacilli → Absent from the lesion
 - The lesion: → Bilateral - Symmetrical - in Crops with tendency to spontaneous healing (Rosacea-like tuberculid) (Lupus miliaris Dissemnatus faciei)
↳ No longer considered as Tuberculoid
- Critia of Diagnosis: • +ve tuberculin test • Evidence of TB elsewhere
• Tuberculoid granuloma in histology • good Response to Drugs

Classes and activities of anti-tuberculous agents

HL

The agent	Spectrum of activity
1st line agents	
Rifampin	Broad
Isoniazid	Tubercle bacilli
Pyrazinamide	Tubercle bacilli
Ethambutol	Tubercle bacilli
Rifapentine	Broad
Rifabutin	Broad
2nd line agents	
Kanamycin, amikacin, streptomycin	Broad
Capreomycin, viomycin	Broad
Levofloxacin, ofloxacin, moxifloxacin, gatifloxacin	Broad
Ethionamide, prothionamide	Tubercle bacilli
Cycloserine, terizidone	Broad
Para-aminosalicylic acid	Tubercle bacilli
3rd line agents	
Clofazimine	Mycobacteria
Amoxicillin/clavulonate	Broad
Linezolid	Broad
Imipenem	Broad
Thiacetazone	Tubercle bacilli
Clarithromycin	Broad

* papulonecrotic tuberculids *

- Lesion: Recurring Symmetrical crops of non-itchy - Dusky Red papules on extensor surface of extremities
- Face, ears, Buttocks
- undergo Central Necrosis
- Heal to pigmented pitted scars -

- Histopathology:
- Early: leukocytoclastic vasculitis
- Later: wedge shape Necrosis to the Base toward the epidermis and perivascular mononuclear infiltrate
- wedge → extruded out → Epithelioid and giant cells → appear at periphery

* lichen scrofulosorum *

- D.P: Grouped - closely set, minute lichenoid, slight scaly, Reddish Brown - perifollicular papules

- Site: Trunk - heal without scarring

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• Histopathology:

- superficial Dermal granulomata → Surround follicles and sweat Ducts
- composed of
 - Epithelioid cells
 - some Langhans giant cells
 - narrow margin of lymphoid cells at periphery
 - No Caseation
- +ve PCR DNA

* Erythema induratum "Bazin" *

- Women more specially w/ T.B and acrocyanosis
- Clinically: persistent, Recurrent → tender nodules on the Back of Lower legs → (calves)
- progress to Ulceration
- The Ulcer: irregular - shallow with Bluish undermined edges
- Healing: with atrophic scars Recurrence: Common
- PF: onset of cold

→ Histopathology:

- Epithelioid cell tubercles in Deep Dermis
- proliferation of walls of Blood vessels and invasion of their walls by inflammatory infiltrate
- "Vasculitis" → Endothelial Swelling + Thrombosis of lumen

Cutaneous tuberculosis* ¹

Disease	Clinical findings	Immunity / Route
Scrofuloderma	Deep nodule typically over cervical lymph node → turns fluctuant & suppurative → ulcerates Heals with prominent scarring	Immunity: sensitized host (low immunity) Route: contiguous spread (from underlying lymphadenitis)
Tuberculous chancre	Painless red-brown papule at inoculation site → non-healing, non-tender undermined ulcer with painless regional lymphadenopathy	Immunity: non-sensitized (no prior immunity) Route: exogenous (direct inoculation); primary infection
Tuberculosis verrucosa cutis (warty TB)	Small indurated hyperkeratotic papule over hand, ankle, or buttock → warty plaque with serpiginous borders Spontaneous resolution with scarring	Immunity: sensitized host (moderate to high immunity) Route: exogenous (direct inoculation at site of trauma); reinfection
Lupus vulgaris	Gelatinous reddish-brown nodules involving face or neck with brown-yellow color ("apple-jelly") on diascopy	Immunity: sensitized host (moderate to high immunity) Route: hematogenous, lymphatic or contiguous
Tuberculosis cutis orificialis	Painful erythematous papule → ulcerates with undermined borders; typically in oral cavity (but can also be genitourinary)	Immunity: sensitized host (impaired cellular immunity) Route: autoinoculation from underlying visceral infection
Miliary tuberculosis	Tiny bluish-red papules (teeming with bacilli) which become crusted; seen mainly in infants or immunosuppressed patients	Immunity: nonsensitized (low immunity) Route: hematogenous dissemination
Tuberculous gumma	Firm, deep seated nodule over trunk, face or extremities → turns soft & fluctuant → ± ulceration	Immunity: immunosuppressed host Route: hematogenous
Papulonecrotic tuberculid	Dusky erythematous papule central necrosis & crust formation	Immunity: sensitized Route: hypersensitivity reaction to distant focus of TB (tuberculid)
Lichen scrofulosorum	Lichenoid tiny papules (tuberculids)	
Erythema induration (Bazin disease)	Subcutaneous inflammatory nodules with ulceration on posterior calves	Associated with past or active TB

* Adapted from: Dermatology, illustrated study guide & comprehensive board review, 2012.

* Atypical Mycobacteria *

(NTM) non tuberculous

- exist → free in the environment ← water
← soil
- M. Tuberculosis, M. leprae → always pathogenic But Atypical mycobacteria have Low Degree of virulence
- PF → is necessary to produce infection ← obstructive pulmonary Disease
← Trauma
← HIV

- They enter human Body By ↑ Inhalation
↑ Skin Trauma
- unlike T.B → Infection with these organisms is acquired from Environment
Not From human source

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Clinical manifestations of non-tuberculous mycobacteria (NTM)²

Clinical manifestations	Common species
1. Chronic pulmonary disease in adults: the most common type of infection	MAC* & <i>M. kansasii</i>
2. Superficial lymphadenitis "mainly cervical": the most common manifestation in children	MAC & <i>M. scrofulaceum</i>
3. Disseminated disease in immunosuppressed patients, e.g. AIDS, lymphomas, cytotoxic drugs, ... etc.	MAC**, <i>M. kansasii</i> & <i>M. hemophilum</i>
4. Cutaneous manifestation: usually produced by inoculation or by dissemination from a distant focus: <ul style="list-style-type: none"> • Swimming pool granuloma & its sporotrichoid variant. • Buruli ulcer. • Subcutaneous nodules, abscesses, plaques & cellulitis-like. 	<i>M. marinum</i> <i>M. ulcerans</i> <i>M. kansasii</i> , <i>M. fortuitum</i> / <i>chelonae</i> , MAC

* MAC = *M. avium* complex consists of 2 species: *M. avium* & *M. intracellulare*

* Swimming pool granuloma *

• D.f: granulomatous Reaction in skin

- Due to: infection $\hat{=}$ M. marinum
- Acquired infection: through minor abrasions occur while Bathing in insufficiently chlorinated swimming pools
- more commonly From: Home aquariums "fish tanks" \rightarrow where the organism is Naturally present

• Clinical:-

- 2-3 weeks after inoculation
- lesion: Solitary Dusky-Red papule or nodule
- site: mainly: fingers, knees, elbow, feet
- \rightarrow slowly Enlarges into Verrucous plaques
- \rightarrow Superficial ulceration occur
- \rightarrow "Sporotrichoid Form" may occur with nodular or ulcerating lesions Along line of: Lymphatic Drainage
- \rightarrow Healing: Spontaneously within 1-3yr

• Diagnosis:-

1- Histopathology \rightarrow Early lesions < 6 months:-

non-specific inflammatory infiltrate

\rightarrow in older lesion: > 6 months:

well formed tuberculoid granulomata with Fibrinoid Necrosis rather than True Caseations

\rightarrow Langhans giant cells \rightarrow occasionally seen

\rightarrow Intracellular acid fast Bacilli (Longer and Broader than M. Tuberculosis) \rightarrow rarely seen

2- Culture \rightarrow +ve in 70% of Cases

3- Tuberculin test \rightarrow +ve But little Value

• Treatment:-

Clarithromycin - Minocycline - Rifampin

Ethambutol - Trimethoprim - Sulfamethoxazole

- 2 agents for serious infection \rightarrow Clarithromycin + Rifampin or Ethambutol
- Combination of rifampin and Ethambutol OR minocycline OR Trimethoprim Sulfamethoxazole OR Clarithromycin OR Azithromycin

* Infectious Causes of lymphocutaneous
"Sporotrichoid" pattern:

- 1- Atypical mycobacteria "M. marinum"
- 2- Sporotrichosis 3- Nocardiosis
- 4- Pyogenic Bacteria (S. aureus)
- 5- Leishmaniasis 6- Tularemia
- 7- Tuberculosis 8- Dimorphic fungi
- 9- opportunistic fungi: Fusarium

• treatment:

- 1- Surgical excision & grafting
- 2- For extensive Disease: combination
of rifampicin + cotrimoxazole +
minocycline
OR Rifampicin + Streptomycin → 4 weeks
- 3- Localized Heat Therapy (M. ulcerans prefer cooler temperature)

* M. Ulcerans "Buruli Ulcer"

• D.f: unusual among mycobacteria → produce
a toxin (mycolactone) → Responsible for clinical
manifestations

• its Acquired → mainly children, after minor Trauma
with an average incubation period of 2 months

• Clinically:

- Itchy . S.C . Firm . Nodule
- Site: mainly on Legs or Forearm
- Break Down to Form → rapidly extending, painless
Shallow necrotic Ulcer & undermined edges
Base of necrotic Fat
- Healing: after few months with prominent Scar
and Contracture formation

• Diagnosis: From Travel History to tropical endemic
area

① Histopathology: granulomatous process with
considerable S.C Fat necrosis

- Clumps of AFB seen in Center of lesion

② Biopsy: from edge of ulcer, numerous extracellular
AFB

③ Buruli Skin test: little Diagnostic

• Leprosy •

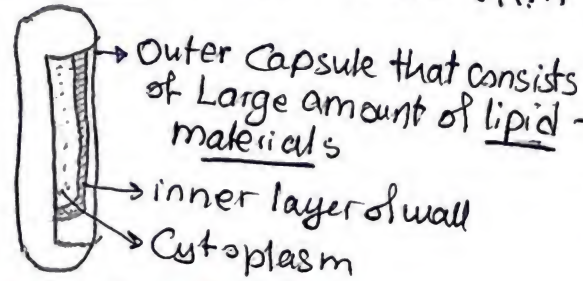
1- Epidemiology:

- more in tropical, Subtropicals areas → Africa → Latin America
→ South East Asia
- ↓ numbers after MDT
- occur in all age groups with Average 10-20 yrs
- children at great risk

2- Etiology:

- Caused By: Mycobacterium leprae
- obligate intracellular parasite
- Stained By: Ziehl-Neelsen as its Acid Fast Bacillus
- it's Doesn't grow in usual media
- Can be inoculated in mice foot pads and in nine Banded armadillo
- M. leprae → Multiplies Slowly → So leprosy Develop slowly months and years

- Structure: Straight Rod 1-8 μm



2 main lipids:

- ① phthiocerol Dimycoserate
 - ② phenolic glycolipid PGL-1
- Shared By other mycobacteria
Specific for M. lepra

3- mode of infection:

- IP = 2-7 yrs
- Occur through → prolonged close contact of suspected individual with an open case of leprosy (untreated phn & multibacillary leprosy & +ve nasal scraping)
- Infection occur through
 - Insect-Bites
 - Feco-oral route
 - Droplet air-borne infection
 - Contact & Ulcerated lesions
 - Blood borne
- Can transmitted through milk of lactating mothers

4- Genetic predisposition:

- 1- Familial Clustering of Cases
- 2- High Concordance rates in identical twins
- 3- associated of HLA-DR2-DR3 with TT, HLA-DQ1 & LL

5-Pathogenesis + classification:

1. most people Develop "Subclinical Infection" and Recover Naturally
2. Few people who Develop "the Disease"
3. The Target is "Neural tissue"
 Schwann cell \rightarrow which engulf the Bacilli and the type of leprosy occur Depend on the Degree of cell mediated immunity (CMI - T cells) of infected ptn.
4. Stimulated T-cells \rightarrow Secrete lymphokines which activate Macrophage to Digest M. Leprae
5. eliminate the Bacilli is made By: Macrophages
 when in Contact w/ M. leprae \rightarrow \uparrow production of Cytokines \leftarrow IL-1, TNF, IL-12 \rightarrow These cytokines stimulate the number and activity of Macrophages
6. predominantly Th1 CD4 T cell Response seen in ptn \leftarrow (TT) \rightarrow producing IL-2 - IFN and TNF \rightarrow That maintain the inflammation

7 - in **LL** → a predominantly Th2 response →
Leads to Release of IL-4 - IL-10 - IL-5 - IL-13
That suppress Macrophage activity

8 - the number of T Cells:

- maximum number present in T T
- Decline in number across leprosy spectrum
- LL → only few lymphocytes are seen

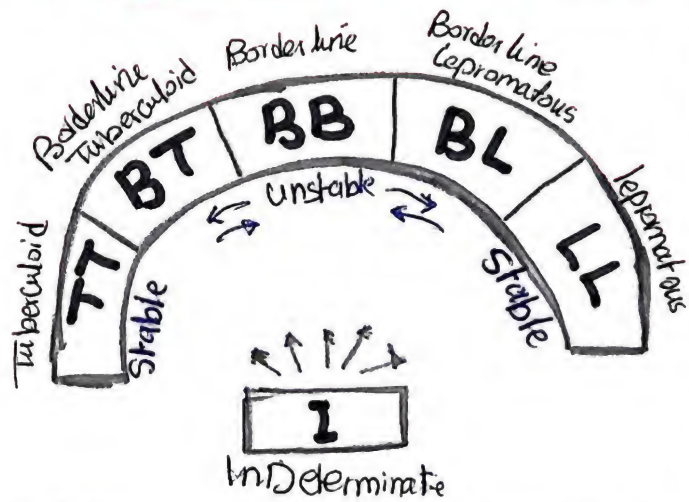
9. **CD₄ Cells and CD₈ Cells:**

- ↳ CD4 cells ↓↓ while that of CD8 cells ↑↑ from tuberculoid to lepromatous end
 ↳ CD4 : CD8 ratio is higher in TT

6- Skin Diseases Based on Th1-Th2

Th 1 - Dominant skin D	Th 2 Dominant skin Diseases
- <u>Tuberculoid leprosy</u>	- <u>Lepromatous leprosy</u>
- <u>Localized leishmaniasis</u>	- <u>Disseminated leishmaniasis</u>
- <u>Allergic Contact Dermatitis</u>	- <u>Acute atopic Dermatitis</u>
- <u>lichen planus</u>	- <u>Advanced CTCL / Sezary</u>
- <u>Early (patch-plaque) CTCL</u>	- <u>Chronic GVHD</u>
- <u>psoriasis</u>	
- <u>Acute GVHD</u>	

7. Spectrum of leprosy:



- 5 Types of leprosy occur forming spectrum
- One pole → Tuberculoid leprosy TT occur in persons with Very High Degree Immunity

→ Followed by BT, BB, BL

- on the other end of spectrum is Lepromatous leprosy LL occur in persons with Very Low immunity

→ Intermediate leprosy is the initial manifestation of leprosy in ptn with undeterminate immunity

- only the two polar form → Stable while all other → Unstable

8- Classification:

① Ridley-Jopling system

→ Depend on host Response to organism

- TT - BT - BB - BL - LL

② WHO system:

→ according to number of lesions

→ and presence of Bacilli on skin smear into :-

Paucibacillary leprosy

- 5 or fewer lesions & absence of organisms on smears

- Tuberculoid - Borderline

Tuberculoid Leprosy

From Ridley-Jopling system

Multibacillary leprosy

- 6 or more lesions & possible visualization of Bacilli on smear

- Lepromatous leprosy - Borderline

lepromatous leprosy, mid Borderline leprosy on Ridley-J. system

9- Leprosy in children:

1- Infants, young children → High risk group in families of infective leprosy ptns → Because of great chance of exposure

2- Mode of infection → Abrasions & Ulcers, Transplacental transmission, mothers milk

3- Clinically → Non lepromatous "paucibacillary" leprosy :- leprosy predominates

→ lepromatous "multibacillary" forms : Uncommon in children

5- Healing : 75% of children with leprosy → Complete Remission in few months without H

Indeterminate

D.F Early Transitory stage • typically seen in: Children ch. ch By:

Clinically Single-Few • Hypochromic - Erythematous Macules - Normal Sensation

Tuberculoid

Develop in • persons e good immunity
→ prevent Dissemination of Bacilli
→ Early Destruction of nerve fibers
→ Few well defined lesions
→ absent Bacilli

Skin: Single-Few. A symmetric Erythematous - Hypopigmented patches, e well-defined elevated Border, tendency to Central clearing Surface → Dry, anhidrotic, hairless e Early Hypoesthesia

• peripheral nerves:

Early → involve TT → wasting paralysis of small muscles of Hand and Feet, anesthesia of limbs trophic changes

The sensation lost in following:
Heat Then Pain Then touch

The involved nerve: thickened Nodular - Tender

- some Cases limited to peripheral nerves only " Neural Type:"

→ Affected nerves:

1. Ulnar
2. Great auricular
3. posterior tibial

Lepromatous

- Develop in: persons e Low CMI

- Early: Skin, mucosal
- Late: neural - Systemic

• Skin: numerous - Bilateral Symmetrical, 3 types

↳ 1. Macular:

numerous - ill defined. Erythematous Hypopigmented Macules

↳ 2. Nodular: skin-colored - pink Copery papules - Nodules

- Smooth, shiny overlying skin

- Sensory changes → slight - absent

- Early nodules → on Face (ears)

↳ any part except warmest parts

- Face " Leonine appearance "

- The outer third eye Brows Lost

- Ichthyosis in lower limbs

↳ 3. Lucio: Diffuse infiltration of Skin Without Nodules

e Alopecia of eye Brows, Eyelashes

Borderline

Immunologically Unstable

- evolve towards:

LL → without Ht

TT → with Ht

Skin: BT

Lesion Similar to TT But smaller - more numerous - less sharply Demarcated

- Small satellite lesion

- Nerve → slight enlarge

BB

- numerous Red plaques ill-defined sloping external edges in LL

- well-defined central Punched out space of normal skin in TT

* Swiss-cheese appearance

BL

- as in LL: numerous macules, papules Not symmetrical

- No Lepromatous features (leonine madorosis)

Indeterminate	Tuberculoid	Lepromatous	Borderline
<p><u>Polarity:</u></p> <p>① if lymphocytes: numerous aggregated around the nerve → lesion doesn't resolve → will develop TT</p> <p>② lymphocytes: scanty ~:~ Bacilli demonstrated lesion → progress to LL</p>	<p>- optic nerve <u>not</u> affected due to absence of schwann sheath</p>	<p>• <u>Nerve Damage</u>: late (after 3-4 yrs) in bilateral pattern → anesthesia - muscle paralysis trophic changes</p> <p>• <u>Mucous membrane</u>: URT e repeated attacks of epistaxis</p> <p>• <u>organs</u>: liver - spleen - L.N - muscle</p>	
<p><u>Histopathology:</u></p> <p>Non-specific inflammatory infiltrate</p>	<p>- Epithelioid cells granulomas (elongated as they follow nerves) e slight admixture of monocytes ↳ giant cells ↳ slight central necrosis</p> <p>- Leptra Bacilli → Abscent</p>	<p>- The infiltrate separated from flattened epidermis by: narrow zone of normal collagen</p> <p>- The infiltrate composed of:- ↳ Macrophages ↳ abundant foamy cytoplasm</p> <p>- Leptra Bacilli → Large numbers in bundles</p>	<p>mixtures of lepromatous and tuberculoid changes</p>
<p><u>Bacteriology:</u></p> <p>Few or No Bacilli</p>	<p>lepra Bacilli Abscent in skin lesion</p>	<p>lepra Bacilli Present in Large number in skin + Nasal smears</p>	<p>lepra Bacilli Can Be Demonstrated But Fewer than LL</p>
<p><u>Immunologically:</u></p> <p><u>Lepromin test:</u></p> <p>Variable Response</p>	<p>lepromin test strongly +ve indicating → High Degree of CMT</p>	<p>-ve lepromin test (Abscent CMI)</p> <p>Anti-bodies to M. leprae antigens Detected in high titre</p> <p>- many Autoantibodies are produced including: Antinuclear - anti-Thyroid anti-syphilitic Reagents</p> <p>- Antibodies in Leprosy Don't have any protective Role → unable to get at the intracellular organism</p>	<p>weak +ve OR Weak -ve</p>

Clinical findings	LL	BL	BB	BT	TT	I
Type of lesions	Macules, papules, nodules, diffuse infiltration	Macules, papules, plaques, infiltration	Plaques & dome-shaped, punched-out lesions	Infiltrated plaques	Infiltrated plaques, often hypopigmented	Macules, often hypopigmented
Number of lesions	Numerous	Many	Many	Single, usually with satellite lesions, to more than 5	One or few (up to 5)	One or few
Distribution	Symmetric	Tendency to symmetry	Evident asymmetry	Asymmetric	Localized, asymmetric	Variable
Definition	Vague, difficult to distinguish normal versus affected skin	Less well-defined borders	Less well-defined borders	Well-defined, sharp borders	Well-defined, sharp borders	Not always defined
Sensation	Not affected	Diminished	Diminished	Absent	Absent	Impaired
Bacilli in skin lesions	Many (globi)	Many	Many	Few (1+), if any, detected	None detected	Usually none detected

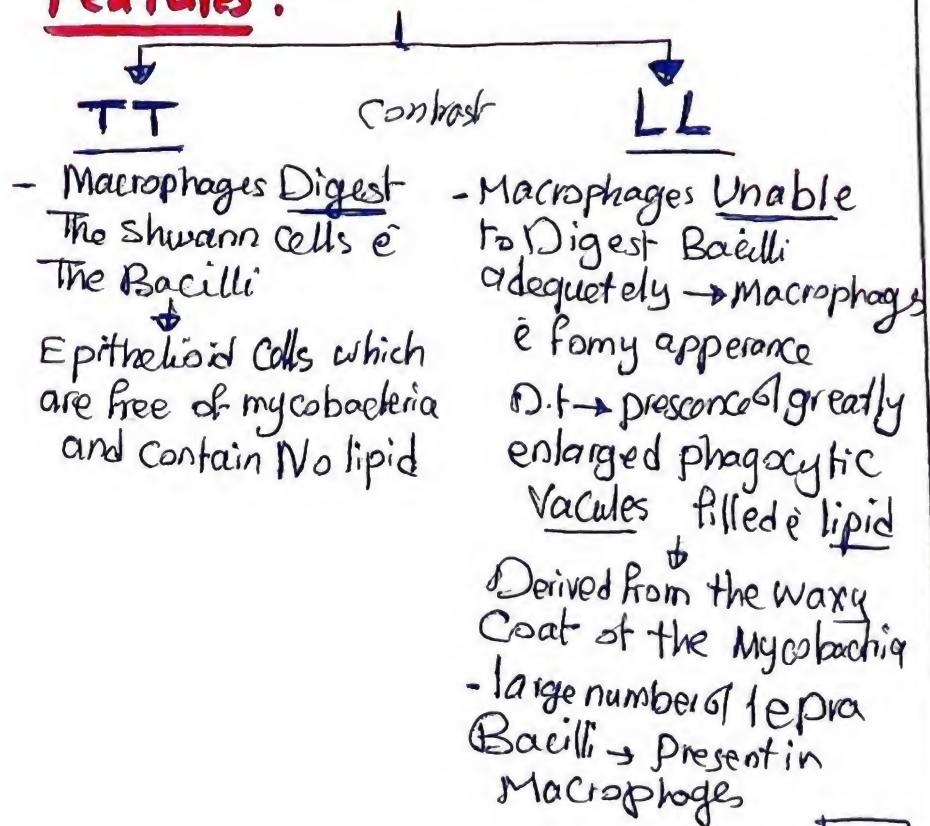
LL, lepromatous leprosy; BL, borderline lepromatous leprosy; BB, mid-borderline leprosy; BT, borderline tuberculoid leprosy; TT, tuberculoid leprosy; I, indeterminate leprosy.

	Tuberculoid (TT)	Borderline (BB)	Lepromatous (LL)
Skin lesions	Single or few, asymmetrical, <u>well-defined</u> erythematous or hypopig. patches, with <u>hypoesthesia</u> , <u>hair loss</u> & <u>anhidrosis</u> & <u>tendency towards central clearing</u> .	Few or several asymmetrical, erythematous, partly well-defined patches, annular & punched-out lesions are characteristic.	Numerous, symmetrical distributed, erythematous or <u>shiny ill-defined macules</u> , papules or nodules. <i>glossening</i> There may be <u>leonine face</u> , loss of <u>eye brows</u> & <u>eye lashes</u> .
Sensory impairment	<u>Marked</u>	<u>Marked in BT</u> , <u>slight in BL</u>	<u>None in early lesions</u>
Peripheral nerves	Single (related to the lesion), enlarged, <u>hard</u> & <u>tender</u> . The condition may be limited to <u>peripheral nerves</u> (neural type).	<u>Several asymmetrically affected</u> .	Many, symmetrically affected, late onset → <u>anesthesia</u> & <u>muscle wasting</u> .
Bacteriology (skin smear)	<u>-ve</u>	<u>Usually +ve</u>	<u>Always +ve</u>
Internal	<u>-ve</u>	<u>-ve</u>	<u>+ve</u>
Lepromin test	<u>Strongly +ve</u>	<u>Weakly +ve</u> (in BT), <u>-ve</u> (in BL).	<u>Always -ve</u>
Skin biopsy	Tubercles of <u>lymphocytes</u> , <u>epithelioid cells</u> & <u>Langhans giant cells</u> in dermis without AFB.	Mixture of <u>tuberculoid</u> & <u>lepromatous features</u> .	<u>Diffuse</u> , <u>spindle-shaped macrophages</u> , <u>foam cells</u> with <u>subepidermal free clear zone</u> .
Course & prognosis	<u>Relatively benign</u> & <u>stable</u> with <u>good prognosis</u>	Unstable may <u>progress</u> to <u>subpolar types</u> , with <u>variable prognosis</u> . Prone to type I reaction.	Most infectious with poor prognosis prone to type II (ENL) reaction.

-10 - Histoid leprosy: ²⁰ lepromatous

- Distinct form of multibacillary leprosy with ch.ch clinical Bacteriological Histopathological feature
- may arise De novo or as a relapse after inadequate leprosy tht
- its tht as multibacillary form

11 - Histogenesis of pathological Features:



12 - HIV infection and leprosy:

- * The effect of HIV infection D.t ↓ ↓ CMI on leprosy:
 - 1 - Conversion of subclinical to Overt leprosy
 - 2 - Induction of Downgrading
 - 3 - Adverse effect on chemotherapy
 - 4 - Promotion of complicating ENL

13 - Nature of immune deficiency in Lepromatous leprosy :-

① Suppressor cell Hypothesis :-

(M. leprae-induced suppressor T. lymphocytes) → are present in peripheral Blood of Lepromatous leprosy Ptn But Not in that of Tuberculoid ptns

② Clonal Deletion hypothesis

(TH cells Reactive to M. leprae) → are defective in Lepromatous leprosy → lead to → inadequate production of IL-2, IFN γ and other lymphokines
- Macrophages → aren't activated and unable to Digest M. leprae

③ Role of Macrophages:

Lepromatous Macrophages defective in (expressing cell surface markers)
↳ in Relasing the T-cell activating IL-2

14 - Reactions in leprosy :

- D.f. During the Chronic Course of leprosy
 - Acute episodes (Reactions) may occur.
 - may occur → Spontaneously or → Precipitated By :
 - effective Hl
 - Intercurrent infections
 - injury
 - physical stress
 - surgical operations
 - pregnancy
 - vaccination against Small Pox
 - HIV

Type I	Type II Erythema Nodosum Leprosum	Type III Lucio phenomenon
<u>Lepromin</u> ↑ Response in Reversal state ↓ Response in Downgrading state	No effect	
<u>pathogenesis</u> • changes in CMI • Comprises upgrading + Downgrading	Immune Complexes → Cutaneous + Systemic small vessel Vasculitis	• in ptn who have Received <u>NO</u> or <u>inadequate</u> Hl • Dense aggregate of Acid fast Bacilli
<u>Type of leprosy</u> • mostly Borderline	mostly LL + BL	• exclusive in Diffuse Lepromatous L
<u>Clinical</u> • Abrupt onset of Erythematous and edematous changes in Old lesions • Tenderness + swelling of <u>nerves</u>	• Acute onset of • Fever • Bilateral + • malaise Symmetrical • arthralgia Erythematous tender <u>Nodules</u> on Face + extensors	* Fever - tenderness - leukocytosis * Abscent - isen limited to Lower extremities, Buttocks, forearm - palpable - Hgic - sharply margined irregular <u>Plaque</u> → Crusts → U/Cor
<u>Histopathology</u> • Shift toward Tubercloid pole in: Reversal Reactions • shift toward Lepromatous pole in: Downgrading Reaction	• Neutrophilic - leukocytoclastic Vasculitis • scanty Fragmented Bacilli around vessels	• <u>VasCular</u> changes → prominent • <u>Endothelial</u> proliferations → luminal Obliteration • <u>Thrombosis</u> of medium vessels • Sparse mononuclear infiltrate

15 - Diagnosis:

1 Slit Skin Smear:

• Site: from suspected lesions or sites
Commonly affected in **LL** ear lobes
forehead
chin
Dorsa of fingers

Technique:

- 1- The lesion \rightarrow cleaned w/ alcohol
- 2- a fold is picked up Between Thumb and Forefinger
- 3- Squeezed tightly to Render it free of Blood
- 4- Small incision made into dermis (5 mm Long - 3 mm deep)
- 5- The Blade then turned at right angles to Cut \rightarrow used to Scrape the Cut surface of tissue.
- 6- Fluid \rightarrow obtained is smeared onto a slide + allowed to Dry (Blood smear is useless)
- 7- Then fixed over a flame and Stained By "modified ZN method"
- 8- Bacilli are seen as Red Rods against Blue Background.

* Bacterial index BI := Density of Bacilli in smear

- \rightarrow helpful in \rightarrow Classification of leprosy
- \rightarrow in Advanced **LL** \rightarrow BI = 5+ or 6+
- \rightarrow the index \downarrow across the spectrum \rightarrow 0-2+ in **BT** leprosy
- \rightarrow Slit skin smear are **-ve** in **TT**
- \rightarrow Under treatment: Bacilli Disappear from **BB** lesions in months
- \rightarrow The last +ve site are:
 - Dorsa of fingers
 - From **BL** lesion in 1-2 yrs
 - From **LL** lesion in 6-10 yrs

* Morphological index MI := percentage of solid staining Bacilli

- \rightarrow These are **Living** Bacilli
- \rightarrow The fragmented and granular Bacilli are **Dead**
- \rightarrow its useful index of progress under treatment
- \rightarrow in **LL** \rightarrow MI reach **Zero** in 4-6 weeks on MDT

Grading of BI

6+ \Rightarrow > 1000 Bacilli
5+ = 100 - 1000
4+ = 10 - 100
3+ = 1 - 10
2+ = 1 - 10 Bacilli / 100 F

Diagnosis in endemic Countries:

\rightarrow Clinically 2 out of 3:

- 1- Anaesthesia \rightarrow in skin lesion or in peripheral nerve Distribution over Dorsal Hands + Feet
- 2- Thickened nerves (at site)
- 3- Typical skin lesions
- 4- By presence of Acid Fast Bacilli in slit skin smear.

[2] Nasal Scrape:

- to Detect → open Case
- Bacilli in nasal mucosa → granular and Disappear in much shorter time
- Examination of Nasal mucosa may also Done

[3] Skin Biopsy :-

- (Deep Biopsy to S.C Fat necessary)
- The Bacilli in leprosy Detected By:
 1. Gram, Ziehl Neelsen, Fite, Wade stain → all stain Bacilli Bright Red
 2. Sudan III + Sudan IV "Scarlet Red Stain" → stain Bacilli Black and Red → respectively بالترتيب
 3. Methenamine silver stain → Detecting fragmented acid fast Bacilli
- 6. 6 sections Be examined in lesions where Bacilli are scanty → to Be Sure Declaring them -ve

[4] Nerve Biopsy:

[2]

[5] Lepromin test:

- "Lepromin" is Crude - Semi standardized preparation of Bacilli from a lepromatous nodule, or infected armadillo liver
- non-specific (not Diagnostic) test
- it's Strongly +ve in TT, weakly +ve in BT
- -ve in BB, BL, LL, unpredictable in indeterminate

- mechanism:

- 0.1 ml of lepromin → injected intradermally
- The site is examined after 48 hrs "Fernandez reaction" or 3-4 weeks → "Mistuda reaction"

↓ +ve Fernandez

- indicate Delayed Hypersensitivity to antigens of M. leprae OR cross reacting reacting mycobacterium

- Interpretation of Mistuda reaction: →

- Nothing = -ve
- < 3 mm papule ± doubtful
- 4-6 mm papule = +ve
- 7-10 mm papule = ++
- > 10 mm nodule or ulceration irrespective of size = +++

↓ +ve Mistuda

- indicate that the person is Capable of mounting an efficient CMR to M. leprae
- e prognostic value
- negativity → can be used as prognostic index to identify people at Risk
- pt in LL → never Become lepromin +ve even if healed

6- Histamine test:

- its Detect the Damage Done to Dermal nerves in Leprosy
- a drop of sulphate of Histamine
- ↓
- applied to Hypochromic Macule and another elsewhere as Control
- as the underlying area is Scarified
- ↓
- The Control area → show triple Response
 - Erythema replaced By a wheel → which later surrounded By large Erythematous Flare
- in Leprosy especially intuberculoid there is No flare.
- in Borderline & indeterminate → the flare is weak + Develop late

7- Pilocarpine test:

- Tincture of iodine → applied to the suspect lesion
- + Normal Skin as a control
- prior to injection of pilocarpine into these sites

- Then These area are Dusted w/ Starch powder → will Turn **BLUE** → if there is **Normal sweating**
- its ↓↓ in lesions of leprosy → as sweating depend on the integrity of parasympathetic nerve fibers

8- SeroDiagnosis:

- 1- antibodies to M. lepra - antigens Highest in LL
Lowest in TT
- 2- ELISA: "Enzyme-Linked Immunosorbent Assay"
For antibodies against phenolic glycolipid:
 - useful Screening test
 - ↓
 - Higher in LL, BL
 - Lower in TT
 - During Chemotherapy
- 3- FLA-Abs
"Fluorescent Leprosy Antibody Absorption test"
- For detection of M. leprae specific antibodies
- 4- RIA: "radioimmuno assay"
- for antibodies to Cell-wall antigen 7 of M. leprae
- 5- PCR: For Detection of M. lepra DNA

16. Treatment of Leprosy:

① Chemotherapy:

Dapsone

- the most important Drug + Cheapest
- Daily adult Dose 100 mg

Rifampicin

- The most potent Bactericidal anti-leprosy
- oral Daily Dose 600 mg 12hr Before food

Clofazimine "Lamprene"

- effective as dapsone
- Mainly Bacteriostatic
- Has anti-inflammatory effect
- Daily oral Dose 50 mg 2 meals or 1 glass of milk

Isoniazid:

= I NH : 175 mg +
Prothionamide : 175 mg +
Dapsone : 50 mg

- 15 - 30 kg = 1 tab/day
- 30 - 50 kg = 2 tab/Day
- > 50 kg = 4 tab/day

2nd generation multiDrug Therapy

- Minocycline = 100 mg/day → for multibacillary ptn / 3 months
↓
Killing all viable M. leprae
- Clarithromycin = 500 mg 1 Day
- Fluoroquinolone (Ciprofloxacin, Ofloxacin) = 400 mg/day / 22 days
→ killing 99.99% of viable M. leprae in multibacillary

Single Drug Combination

- (Rifampicin + Ofloxacin + Minocycline)

- tried For ptn with single skin lesion

- also WHO recommended for paucibacillary leprosy with single skin lesion

- MultiDrug Therapy Regimens MDT

in adults: → □ paucibacillary leprosy (I-TT-BT)

- Daily • at Home → Dapsone 100 mg
- monthly • undersupervision → Rifampicin 600 mg
- Duration = 6 months

→ Multi bacillary (BB-BL-LL)

- Daily • at Home → Dapsone 100 mg + Clofazimine 50 mg
- monthly • undersupervision → Rifampicin 600 mg + Clofazimine 300 mg
- Duration = 2 yr → until -ve

For single paucibacillary
Single dose
- Rifampicin 600 mg
- Ofloxacin 400 mg
- Minocycline 100 mg

II Treatment of reactions:

- Precipitated Factors:
Should avoided

Immunization
pregnancy
intercurrent infection

- Chemotherapy → Continued as usual

- mild Reactions →

Aspirin 600 mg / 4-6 hrs

Chloroquine 150 mg / 8 hr

Type II

• Thalidomide 400 mg

- at night

- Never to women in child-bearing period
C-teratogenic

• Clofazimine 300 mg

- Daily

- Reduce Dose gradually to normal within 2 months to avoid Toxicity

• Prednisone 300 mg

- initially

- if Thalidomide is Contra

Type I

• prednisone starting
50-80 mg / daily

↓
Gradually Reducing
The Dose Specially in
Sever Cases of Neuritis
& Iridocyclitis

↓
Ht with hourly Then
4 hourly =

1% Hydrocortisone
eye Drops

+
atropine 1%

+
Scopolamine 0.5%

24

III Educate the ptn:

- to cope w/ anesthetic Hand or Foot

(e.g) Daily inspection for warmth + Bruising
Wearing gloves at work, Avoid Burning heat

IV Ht of complication of Nerve Damage:

- Anesthesia: well-fitting shoe (specially if presence of Deformities)
- Rest → if injury or ulcer
- Physiotherapy: weakness or paralysis

V Prevention + Control:

1. Health education
2. Early Case Detection
3. Early Ht & Chemotherapy "MDT"
4. Child Contacts of lepromatous Cases:-
Benefit from prophylactic chemotherapy 6 months (pauci)
5. Vaccination:
 - BCG (Cultivable mycobacterium)
 - killed M. leprae isolated from experimentally armadillos
 - killed M. leprae + BCG
 - Recombinant vaccine By genetic engineering of DNA

	Erythema nodosum	Erythema induratum of Bazin
CP	<ul style="list-style-type: none"> - The most common cause of panniculitis (septal panniculitis without vasculitis) - Multiple, bilateral, symmetrical, tender, warm, red nodules on shins of tibia, may be on thigh or forearm - Spontaneous healing with bruise-like appearance without ulceration or scarring - Acute course , recurrent - Fever, malaise, arthralgia, leukocytosis 	<ul style="list-style-type: none"> - Usually affects women who have TB - Tender, nodules on the back of lower legs, calves - It may ulcerate → irregular, shallow, bluish undermined edge ulcer, healing with atrophic scar - Persistent or recurrent
Pathogenesis	<ul style="list-style-type: none"> - Reactive erythema to many etiological factors: streptococcal infection, drugs, sarcoidosis, TB - May be due to immune complex 	<ul style="list-style-type: none"> - It may be tuberculid - Past or active foci of TB may be present
HP	<ul style="list-style-type: none"> - Deep skin biopsy - Septal inflammatory infiltrate - Septal vascular endothelial swelling - Edema & hge - Predominance of lymphocytes, histiocytes & giant cells - No leukocytoclastic vasculitis - No fat necrosis 	<ul style="list-style-type: none"> - Epithelioid cell tubercles in deep dermis - Proliferation of walls of blood vessels & inflammatory infiltrate (vasculitis) → endothelial swelling + thrombosis → occlusion & necrosis
ttt	<ol style="list-style-type: none"> 1- The cause 2- Bed rest 3- NSAID 4- K iodide 	<ol style="list-style-type: none"> 1- AntiTB 2- Dapsone 3- Systemic steroid

	Scrofuloderma	Lichen scrofulosorum
Etiology	Direct extension to the skin from underlying tuberculous focus, LN, bone, joint, epididymis	Hematogenous dissemination of tubercle bacilli from a distant source → delayed type hypersensitivity response Tuberculid
Tuberculin test	+ve	+ve
bacilli	Present in the lesion	Absent in the lesion
CP	Bluish red, nodule → ulcer with bluish undermined edges & floor covered with soft granulation tissue, sinuses & fistulae may present ,	Bilateral, symmetrical, grouped, closely set, minute lichenoid, slightly scaly, reddish brown, perifollicular papules, trunk
Healing	scarring → irregular adherent masses, puckered scarring	Without scarring
HP	Tuberculous granulation tissue with caseation necrosis in deeper tissue, bacilli may be found	Superficial dermal granuloma surrounds follicles & sweat ducts composed of epithelioid cells with some langhans giant cells & a narrow margin of lymphoid cells at the periphery, no caseation
ttt	Antituberculous drugs	

* ESR > 100

- 1- TB
- 2- Collagen Disease
- 3- Malignancy

* Asteroid Bodies:

- 1- TB
- 2- Leprosy
- 3- Sarcoidosis

* Diseases Caused By Cat:

- 1- Mycobacterial: TB
- 2- Bacterial: Cat scratch D
- Cellulitis
- 3- parasite: Scabies
- 4- Fungal: Dermatophytes
- 5- atopic Dermatitis -
- 6- Urticaria

* Cicatricial alopecia:

* Infections:

- Mycobact: LV. Leprosy
- fungal: Kerion-favus
- Protozoa: leishmaniasis

* Congenital eg: Darier D

* Traumatic: Trauma, Burn

* Tumor: BCC, SCC.

* Hypopigmented macules on trunk:

- 1- Tuberculoid leprosy
- 2- morphea
- 3- Vitiligo
- 4- syphilis
- 5- pityriasis alba
- 6- Nevus Depigmentosus
- 7- Tinea versicolor

* loss of outer one third of eyebrow:

- 1- Leprosy
- 2- myxedema
- 3- Trichotellomania
- 4- alopecia areata

* Leonine face:

- 1- Leprosy (LL)
- 2- leishmaniasis
- 3- Sarcoidosis
- 4- Systemic amyloidosis
- 5- lipoid proteinosis
- 6- Scleromyxedema
- 7- lymphoma cutis
- 8- leukemia cutis
- 9- Nodular mastocytosis
- 10- Histocytosis
- 11- Actinic Dermatitis

Q Mycobacterial Infections:

- 1- Mention 3 diseases caused by M. tuberculosis.
- 2- Tuberculosis cutis.
- 3- Naked tubercle.
- 4- Orificial tuberculosis: DD, investigations, ttt.
- 5- Cutaneous tuberculosis: clinical varieties, pathology, management.
- 6- Tuberculosis verrucosa cutis.
- 7- Lupus vulgaris: histopathology, diagnosis & ttt.
- 8- Management of lupus vulgaris.

- 9- Classification & Clinical types of leprosy.
- 10- Clinical features of leprosy.
- 11- Spectrum of leprosy & diagnosis.
- 12- Borderline leprosy.
- 13- Clinical manifestations of paucibacillary leprosy.
- 14- Histopathology of leprosy.
- 15- Compare: histopathological features of tuberculoid leprosy & lepromatous leprosy.
- 16- Lepra reactions.
- 17- Compare: type 1 & 2 lepra reactions.
- 18- Investigations of lepromatous leprosy.
- 19- Lab investigation & ttt of multibacillary leprosy & lupus vulgaris.
- 20- Management & complications of lepromatous leprosy.
- 21- Diagnostic procedures of suspected case of leprosy.
- 22- WHO therapy of leprosy.
- 23- First line of systemic ttt of tuberculoid leprosy.
- 24- Treatment of leprosy.